Complete Summary

GUIDELINE TITLE

Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America.

BIBLIOGRAPHIC SOURCE(S)

Pappas PG, Kauffman CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr, Filler SG, Fisher JF, Kullberg BJ, Ostrosky-Zeichner L, Reboli AC, Rex JH, Walsh TJ, Sobel JD, Infectious Diseases Society of America. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009 Mar 1;48(5):503-35. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Pappas PG, Rex JH, Sobel JD, Filler SG, Dismukes WE, Walsh TJ, Edwards JE. Guidelines for treatment of candidiasis. Clin Infect Dis 2004 Jan 15;38(2):161-89. [344 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Candidemia, other forms of invasive candidiasis, and mucosal candidiasis, including:

- Candidemia in non-neutropenic and neutropenic patients
- Suspected invasive candidiasis in non-neutropenic and neutropenic patients

- Urinary tract infections due to *Candida* (asymptomatic and symptomatic candiduria)
- Vulvovaginal candidiasis
- Chronic disseminated candidiasis
- Osteoarticular *Candida* infections
- Central nervous system (CNS) candidiasis
- *Candida* endophthalmitis
- *Candida* infections of the cardiovascular system
- Neonatal candidiasis
- Oropharyngeal and esophageal candidiasis

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Risk Assessment
Treatment

CLINICAL SPECIALTY

Cardiology
Critical Care
Gastroenterology
Hematology
Infectious Diseases
Internal Medicine
Neurological Surgery
Neurology
Obstetrics and Gynecology
Oncology
Ophthalmology
Orthopedic Surgery
Pediatrics
Pulmonary Medicine
Surgery
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Nurses
Pharmacists
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

- To summarize current knowledge and provide recommendations for the treatment of multiple forms of candidiasis, including invasive and mucocutaneous candidiasis

- To present prophylactic strategies for the prevention of invasive candidiasis in at-risk patients
- To update the January 2004 clinical practice guidelines on the management of candidiasis

TARGET POPULATION

Patients who either have or are at risk for invasive candidiasis and mucosal candidiasis

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment/Prevention/Management

1. Treatment (including empirical therapy) and antifungal prophylaxis with:
    - Amphotericin B (AmB)
    - Triazoles
    - Echinocandins
    - Flucytosine
2. Use of adult and pediatric dosing for antifungal agents
3. Considerations during pregnancy
4. Therapeutic drug monitoring
5. Antifungal susceptibility testing to guide management
6. Non-culture-based diagnostic techniques
7. Specific therapy for each condition or treatment group (see "Major Recommendations" field)

MAJOR OUTCOMES CONSIDERED

- Effectiveness of treatment (clearance of *Candida*, symptom resolution)
- Toxicity of antifungal treatment
- Recurrence rate
- Mortality
- Incidence of invasive candidiasis

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

For the 2009 update, the Expert Panel completed the review and analysis of data published since 2004. Computerized literature searches of the English-language literature using PubMed were performed.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence	
I	Evidence from ≥1 properly randomized, controlled trial.
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Adapted from Canadian Task Force on the Periodic Health Examination.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

In evaluating the evidence regarding the management of candidiasis, the Expert Panel followed a process used in the development of other Infectious Diseases Society of America (IDSA) guidelines. The process included a systematic weighting of the quality of the evidence and the grade of recommendation (see "Rating Scheme for the Strength of the Evidence" and "Rating Scheme for the Strength of the Recommendations" fields).

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Expert Panel met in person on 1 occasion and via teleconference 11 times to discuss the questions to be addressed, to make writing assignments, and to deliberate on the recommendations. All members of the Expert Panel participated in the preparation and review of the draft guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Strength of Recommendation

Category/Grade	Definition
Strength of Recommendation	
A	Good evidence to support a recommendation for or against use.
B	Moderate evidence to support a recommendation for or against use.
C	Poor evidence to support a recommendation.

Adapted from Canadian Task Force on the Periodic Health Examination.

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Feedback from external peer reviews was obtained. The guidelines were reviewed and approved by the Infectious Diseases Society of America (IDSA) Standards and Practice Guidelines Committee (SPGC) and the IDSA Board of Directors prior to dissemination.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the Infectious Diseases Society of America (IDSA): There have been several significant changes in the management of candidiasis since the last publication of these guidelines in January 2004. Most of these changes relate to the appropriate use of echinocandins and expanded spectrum azoles in the management of candidemia, other forms of invasive candidiasis, and mucosal candidiasis. For some of the less common forms of invasive candidiasis (e.g., chronic disseminated candidiasis, osteomyelitis, and central nervous system [CNS] disease), there are few new treatment data since 2004, with only anecdotal experience, case reports, or small series providing some evidence to support new approaches to therapy. Each section of the Guideline begins with a specific clinical question and is followed by numbered recommendations. A summary of the most-relevant evidence in support of the recommendations for each question can be found in the original guideline document.

Ratings of quality of evidence (**I-III**) and strength of recommendation (**A-C**) are defined at the end of the "Major Recommendations" field.

What Is the Treatment of Candidemia in Non-neutropenic Patients?

1. Fluconazole (loading dose of 800 mg [12 mg/kg], then 400 mg [6 mg/kg] daily) or an echinocandin (caspofungin: loading dose of 70 mg, then 50 mg daily; micafungin: 100 mg daily; anidulafungin: loading dose of 200 mg, then 100 mg daily) is recommended as initial therapy for most adult patients (**A-I**). The Expert Panel favors an echinocandin for patients with moderately severe to severe illness or patients who have had recent azole exposure (**A-III**). Fluconazole is recommended for patients who are less critically ill and who have no recent azole exposure (**A-III**). The same therapeutic approach is advised for children, with attention to differences in dosing regimens (**B-III**).
2. Transition from an echinocandin to fluconazole is recommended for patients who have isolates that are likely to be susceptible to fluconazole (e.g., *Candida [C] albicans*) and who are clinically stable (**A-II**).
3. For infection due to *C. glabrata*, an echinocandin is preferred (**B-III**). Transition to fluconazole or voriconazole is not recommended without confirmation of isolate susceptibility (**B-III**). For patients who initially received fluconazole or voriconazole, are clinically improved, and whose follow-up culture results are negative, continuing an azole to completion of therapy is reasonable (**B-III**).
4. For infection due to *C. parapsilosis*, fluconazole is recommended (**B-III**). For patients who have initially received an echinocandin, are clinically improved, and whose follow-up culture results are negative, continuing use of an echinocandin is reasonable (**B-III**).
5. Amphotericin B-deoxycholate (AmB-d) (0.5–1.0 mg/kg daily) or a lipid formulation of AmB (LFAmB) (3–5 mg/kg daily) are alternatives if there is intolerance to or limited availability of other antifungal agents (**A-I**). Transition from AmBd or LFAmB to fluconazole therapy is recommended for patients who have isolates that are likely to be susceptible to fluconazole (e.g., *C. albicans*) and who are clinically stable (**A-I**).
6. Voriconazole (400 mg [6 mg/kg] twice daily for 2 doses, then 200 mg [3 mg/kg] twice daily) is effective for candidemia (**A-I**), but it offers little advantage over fluconazole and is recommended as step-down oral therapy for selected cases of candidiasis due to *C. krusei* or voriconazole-susceptible *C. glabrata* (**B-III**).
7. Recommended duration of therapy for candidemia without obvious metastatic complications is for 2 weeks after documented clearance of *Candida* species from the bloodstream and resolution of symptoms attributable to candidemia (**A-III**).
8. Intravenous catheter removal is strongly recommended for nonneutropenic patients with candidemia (**A-II**).

What Is the Treatment of Candidemia in Neutropenic Patients?

9. An echinocandin (caspofungin, loading dose of 70 mg, then 50 mg daily; micafungin, 100 mg daily (**A-II**); anidulafungin, loading dose of 200 mg, then 100 mg daily (**A-III**)) or lipid formulation of amphotericin B (LFAmB) (3–5 mg/kg daily) (**A-II**) is recommended for most patients.
10. For patients who are less critically ill and who have no recent azole exposure, fluconazole (800 mg [12 mg/kg] loading dose, then 400 mg [6 mg/kg] daily) is a reasonable alternative (**B-III**). Voriconazole (400 mg [6 mg/kg] twice

daily for 2 doses, then 200 mg [3 mg/kg] twice daily) can be used in situations in which additional mold coverage is desired (**B-III**).

11. For infections due to *C. glabrata*, an echinocandin is preferred (**B-III**); LFAmB is an effective but less attractive alternative because of cost and the potential for toxicity (**B-III**). For patients who were already receiving voriconazole or fluconazole, are clinically improved, and whose follow-up culture results are negative, continuing use of the azole to completion of therapy is reasonable (**B-III**).
12. For infections due to *C. parapsilosis*, fluconazole or LFAmB is preferred as initial therapy (**B-III**). If the patient is receiving an echinocandin and is clinically stable and if follow-up culture results are negative, continuing use of the echinocandin until completion of therapy is reasonable. For infections due to *C. krusei*, an echinocandin, LFAmB, or voriconazole is recommended (**B-III**).
13. Recommended duration of therapy for candidemia without persistent fungemia or metastatic complications is 2 weeks after documented clearance of *Candida* from the bloodstream and resolution of symptoms attributable to candidemia and resolution of neutropenia (**A-III**).
14. Intravenous catheter removal should be considered (**BIII**).

What Is the Empirical Treatment for Suspected Invasive Candidiasis in Non-neutropenic Patients?

15. Empirical therapy for suspected candidiasis in nonneutropenic patients is similar to that for proven candidiasis. Fluconazole (800-mg [12-mg/kg] loading dose, then 400 mg [6 mg/kg] daily), caspofungin (70-mg loading dose, then 50 mg daily), anidulafungin (200-mg loading dose, then 100 mg daily), or micafungin (100 mg daily) is recommended as initial therapy (**B-III**). An echinocandin is preferred for patients with recent azole exposure, patients with moderately severe to severe illness, or patients who are at high risk of infection due to *C. glabrata* or *C. krusei* (**B-III**).
16. AmB-d (0.5–1.0 mg/kg daily) or LFAmB (3–5 mg/kg daily) are alternatives if there is intolerance to other antifungals or limited availability of other antifungals (**B-III**).
17. Empirical antifungal therapy should be considered in critically ill patients with risk factors for invasive candidiasis and no other known cause of fever and should be based on clinical assessment of risk factors, serologic markers for invasive candidiasis, and/or culture data from nonsterile sites (**B-III**).

What Is the Empirical Treatment for Suspected Invasive Candidiasis in Neutropenic Patients?

18. LFAmB (3–5 mg/kg daily), caspofungin (70-mg loading dose, then 50 mg daily) (**A-I**), or voriconazole (6 mg/kg twice daily for 2 doses, then 3 mg/kg twice daily) are recommended (**B-I**).
19. Fluconazole (800-mg [12-mg/kg] loading dose, then 400 mg [6 mg/kg] daily) and itraconazole (200 mg [3mg/kg] twice daily) are alternative agents (**B-I**).
20. AmB-d is an effective alternative, but there is a higher risk of toxicity than there is with LFAmB (**A-I**).
21. Azoles should not be used for empirical therapy in patients who have received an azole for prophylaxis (**B-II**).

What Is the Treatment for Urinary Tract Infections Due to *Candida* Species?

Recommendations: Asymptomatic Candiduria

22. Treatment is not recommended unless the patient belongs to a group at high risk of dissemination (**A-III**). Elimination of predisposing factors often results in resolution of candiduria (**A-III**).
23. High-risk patients include neutropenic patients, infants with low birth weight, and patients who will undergo urologic manipulations. Neutropenic patients and neonates should be managed as described for invasive candidiasis. For those patients undergoing urologic procedures, fluconazole administered at a dosage of 200-400 mg (3–6 mg/kg) daily or AmB-d administered at a dosage of 0.3–0.6 mg/kg daily for several days before and after the procedure is recommended (**B-III**).
24. Imaging of the kidneys and collecting system to exclude abscess, fungus ball, or urologic abnormality is prudent when treating asymptomatic patients with predisposing factors (**B-III**).

Recommendations: Symptomatic Candiduria

25. For candiduria with suspected disseminated candidiasis, treatment as described for candidemia is recommended (**AIII**).
26. For cystitis due to a fluconazole-susceptible *Candida* species, oral fluconazole at a dosage of 200 mg (3 mg/kg) daily for 2 weeks is recommended (**A-III**). For fluconazole-resistant organisms, AmB-d at a dosage of 0.3–0.6 mg/kg daily for 1–7 days or oral flucytosine at a dosage of 25 mg/kg 4 times daily for 7–10 days are alternatives (**B-III**). AmB-d bladder irrigation is generally not recommended but may be useful for treatment of patients with fluconazole-resistant *Candida* species, especially *C. glabrata* (**B-III**).
27. For pyelonephritis due to fluconazole-susceptible organisms, oral fluconazole at a dosage of 200–400 mg (3–6 mg/kg) daily for 2 weeks is recommended (**B-III**). For patients with fluconazole-resistant *Candida* strains, especially *C. glabrata*, alternatives include AmB-d at a dosage of 0.5–0.7 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily (**B-III**), or flucytosine alone at a dosage of 25 mg/kg 4 times daily (**B-III**) for 2 weeks.
28. For fungus balls, surgical intervention is strongly recommended in nonneonates (**B-III**). Fluconazole at a dosage of 200–400 mg (3–6 mg/kg) daily is recommended (**B-III**). AmBd at a dosage of 0.5–0.7 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily is an alternative (**B-III**). If access to the renal collecting system is available, an adjunct to systemic therapy is irrigation with AmB-d at a concentration of 50 mg/L of sterile water (**B-III**). Treatment duration should be until symptoms have resolved and urine cultures no longer yield *Candida* species (**B-III**).

What Is the Treatment for Vulvovaginal Candidiasis (VVC)?

29. Several topical antifungal agents are effective therapy for VVC, and no agent is clearly superior (see table 4 in the original guideline document) (**A-I**).
30. A single 150-mg dose of fluconazole is recommended for the treatment of uncomplicated *Candida* VVC (**A-I**).

31. For recurring *Candida* VVC, 10–14 days of induction therapy with a topical or oral azole, followed by fluconazole at a dosage of 150 mg once per week for 6 months, is recommended (**A-I**).

What Is the Treatment for Chronic Disseminated Candidiasis?

32. Fluconazole at a dosage of 400 mg (6 mg/kg) daily is recommended for clinically stable patients (**A-III**). LFAmB at a dosage of 3–5 mg/kg daily or AmB-d at a dosage of 0.5–0.7 mg/kg daily can be used to treat acutely ill patients or patients with refractory disease (**A-III**). Induction therapy with AmB for 1–2 weeks, followed by oral fluconazole at a dosage of 400 mg (6 mg/kg) daily, is also recommended (**B-III**).
33. Anidulafungin (loading dose of 200 mg, then 100 mg daily), micafungin (100 mg daily), or caspofungin (loading dose of 70 mg, then 50 mg daily for 1–2 weeks) are alternatives for initial therapy, followed by oral fluconazole when clinically appropriate (**B-III**).
34. Therapy should be continued for weeks to months, until calcification occurs or lesions resolve (**A-III**). Premature discontinuation of antifungal therapy can lead to recurrent infection.
35. Patients with chronic disseminated candidiasis who require ongoing chemotherapy or undergo stem cell transplantation should continue to receive antifungal therapy throughout the period of high risk to prevent relapse (**A-III**).

What Is the Treatment for Osteoarticular Candida Infections?

36. For osteomyelitis, the Expert Panel recommends fluconazole at a dosage of 400 mg (6 mg/kg) daily for 6–12 months or LFAmB at a dosage of 3–5 mg/kg daily for at least 2 weeks, followed by fluconazole at a dosage of 400 mg daily for 6–12 months (**B-III**). Alternatives include an echinocandin or AmB-d at a dosage of 0.5–1 mg/kg daily for at least 2 weeks, followed by fluconazole at a dosage of 400 mg daily for 6–12 months (**B-III**). Surgical debridement in selected cases is advised (**B-III**).
37. For septic arthritis, the Expert Panel recommends treatment for at least 6 weeks with fluconazole at a dosage of 400 mg (6 mg/kg) daily or LFAmB at a dosage of 3–5 mg/kg daily for at least 2 weeks, followed by fluconazole at a dosage of 400 mg daily (**B-III**). Alternatives include an echinocandin or AmB-d at a dosage of 0.5–1 mg/kg daily for at least 2 weeks, followed by fluconazole at a dosage of 400 mg daily for the remainder of therapy (**B-III**). Surgical debridement is indicated in all cases (**A-III**).
38. For infection involving a prosthetic device, device removal is recommended for most cases (**A-III**). Therapy for at least 6 weeks with the above dosages of fluconazole, LFAmB, an echinocandin, or AmB-d is recommended (**B-III**). If the device cannot be removed, chronic suppression with fluconazole is recommended (**B-III**).

What Is the Treatment for Central Nervous System (CNS) Candidiasis in Adults?

39. LFAmB at a dosage of 3–5 mg/kg daily, with or without flucytosine at a dosage of 25 mg/kg 4 times daily, is recommended for the initial several weeks of treatment (**B-III**).

40. Fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily is recommended as step-down therapy after the patient responds to initial treatment with LFAmB and flucytosine. Therapy should continue until all signs and symptoms, cerebrospinal fluid (CSF) abnormalities, and radiologic abnormalities have resolved (**B-III**).
41. Removal of infected ventricular devices is recommended (**A-III**).

What Is the Treatment for Candida Endophthalmitis?

42. AmB-d at a dosage of 0.7–1 mg/kg daily, combined with flucytosine at a dosage of 25 mg/kg administered 4 times daily, is recommended for advancing lesions or lesions threatening the macula (**A-III**). Fluconazole at a dosage of 400–800 mg daily (loading dose of 12 mg/kg then 6–12 mg/kg daily) is an acceptable alternative for less severe endophthalmitis (**B-III**). LFAmB at a dosage of 3–5 mg/kg daily, voriconazole at a dosage of 6 mg/kg twice daily for 2 doses and 3–4 mg/kg twice daily thereafter, or an echinocandin can be used to treat patients who are intolerant of or experiencing treatment failure with AmB-d in combination with flucytosine or fluconazole (**B-III**).
43. The recommended duration of therapy is at least 4–6 weeks and is determined by the stabilization or resolution of lesions as documented by repeated ophthalmological examinations (**A-III**).
44. All patients with candidemia should have at least 1 dilated retinal examination early in the course of therapy, preferably performed by an ophthalmologist (**A-II**). It is especially important to examine patients who cannot communicate regarding visual disturbances.
45. A diagnostic vitreal aspirate is recommended for patients with endophthalmitis of unknown origin (**A-III**). The Expert Panel strongly recommends ophthalmologic consultation for consideration of partial vitrectomy and intravitreal antifungal therapy with AmB-d for all patients with severe endophthalmitis and vitreitis (**B-III**).

What Is the Treatment for Candida Infections of the Cardiovascular System?

46. For native valve endocarditis, LFAmB at a dosage of 3– 5 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily is recommended (**B-III**). Alternatives include AmB-d at a dosage of 0.6–1 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily or an echinocandin (higher dosages may be necessary than for treatment of candidemia; e.g., caspofungin at a dosage of 50–150 mg daily, micafungin at a dosage of 100–150 mg daily, or anidulafungin at a dosage of 100–200 mg daily) (**B-III**). Step-down therapy to fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily should be considered among patients with susceptible *Candida* isolates who have demonstrated clinical stability and clearance of *Candida* from the bloodstream (**B-III**). Valve replacement is recommended, and treatment should continue for at least 6 weeks after valve replacement and should continue for a longer duration in patients with perivalvular abscesses and other complications (**B-III**).
47. For patients who cannot undergo valve replacement, long-term suppression with fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily is recommended (**B-III**).

48. For prosthetic valve endocarditis (PVE), the recommendations above apply, and suppressive therapy should be lifelong if valve replacement is not possible (**B-III**).
49. For pericarditis, LFAmB at a dosage of 3–5 mg/kg daily, AmB-d at a dosage of 0.6–1 mg/kg daily, an echinocandin administered at the dosages noted in recommendation 46, or fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily for as long as several months, in combination with either a pericardial window or pericardiectomy, is recommended (**B-III**). Step-down therapy to fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily should be considered for patients who have initially responded to AmB or an echinocandin and who are clinically stable (**B-III**).
50. For myocarditis, treatment as for endocarditis (as outlined in recommendation 46) is recommended (**B-III**).
51. For suppurative thrombophlebitis, catheter removal and incision and drainage or resection of the vein, if feasible, is recommended **(B-III**). LFAmB at a dosage of 3–5 mg/kg daily, AmB-d at a dosage of 0.6–1 mg/kg daily, fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily, or an echinocandin at the dosages noted in recommendation 46 for at least 2 weeks after candidemia has cleared is recommended (**B-III**). Step-down therapy to fluconazole at a dosage of 400–800 mg (6–12 mg/ kg) daily should be considered for patients who have initially responded to AmB or an echinocandin and who are clinically stable (**B-III**). Resolution of the thrombus can be used as evidence to discontinue antifungal therapy if clinical and culture data are supportive (**B-III**).
52. For pacemaker and implantable cardiac defibrillator wire infections, removal of the entire device and systemic antifungal therapy with LFAmB at a dosage of 3–5 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily, AmB-d at a dosage of 0.6–1 mg/kg daily with or without flucytosine at a dosage of 25 mg/kg 4 times daily, or an echinocandin at the dosages noted in recommendation 46 is recommended (**B-III**). Step-down therapy to fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily should be considered for patients with susceptible *Candida* isolates who have demonstrated clinical stability and clearance of *Candida* from the bloodstream (**B-III**). For infections limited to generators and/or pockets, 4 weeks of antifungal therapy after removal of the device is recommended (**B-III**). For pacemaker and implantable cardiac defibrillator wire infections, at least 6 weeks of antifungal therapy after wire removal is recommended (**B-III**).
53. For ventricular assist devices that cannot be removed, treatment with LFAmB, AmB-d, or an echinocandin at the dosages noted in recommendation 46 is recommended (**B-III**). After candidemia has cleared and the patient has responded clinically, fluconazole at a dosage of 400–800 mg (6–12 mg/kg) daily is recommended as step-down therapy (**B-III**). Chronic suppressive therapy with fluconazole is warranted until the device is removed (**B-III**).

What Is the Treatment for Neonatal Candidiasis?

54. AmB-d at a dosage of 1 mg/kg daily is recommended for neonates with disseminated candidiasis (**A-II**). If urinary tract involvement is excluded, LFAmB at a dosage of 3–5 mg/kg daily can be used (**B-II**). Fluconazole at a dosage of 12 mg/kg daily is a reasonable alternative (**B-II**). The recommended length of therapy is 3 weeks (**B-II**).

55. A lumbar puncture and a dilated retinal examination are recommended in neonates with sterile body fluid and/or urine cultures positive for *Candida* species (**B-III**). Imaging of the genitourinary tract, liver, and spleen should be performed if sterile body fluid cultures have persistently positive results (**B-III**).
56. Echinocandins should be used with caution and generally limited to situations in which resistance or toxicity preclude the use of fluconazole or AmB-d (**B-III**).
57. Intravascular catheter removal is strongly recommended (**A-II**).
58. In nurseries with high rates of invasive candidiasis, fluconazole prophylaxis may be considered in neonates with birth weights <1000 g (**A-I**). Antifungal drug resistance, drug-related toxicity, and neurodevelopmental outcomes should be observed (**A-III**).

What Is the Significance of Candida Isolated from Respiratory Secretions?

59. Growth of *Candida* from respiratory secretions rarely indicates invasive candidiasis and should not be treated with antifungal therapy (**A-III**).

What Is the Treatment for Nongenital Mucocutaneous Candidiasis?

Recommendations: Oropharyngeal Candidiasis

60. For mild disease, clotrimazole troches at a dosage of 10 mg 5 times daily, nystatin suspension at a concentration of 100,000 U/mL and a dosage of 4–6 mL 4 times daily, or 1–2 nystatin pastilles (200,000 U each) administered 4 times daily for 7–14 days is recommended (**B-II**).
61. For moderate to severe disease, oral fluconazole at a dosage of 100–200 mg (3 mg/kg) daily for 7–14 days is recommended (**A-I**).
62. For fluconazole-refractory disease, either itraconazole solution at a dosage of 200 mg daily or posaconazole suspension at a dosage of 400 mg twice daily for 3 days, then 400 mg daily for up to 28 days, are recommended (**A-II**). Voriconazole at a dosage of 200 mg twice daily or a 1-mL oral suspension of AmB-d, administered at a dosage of 100 mg/mL 4 times daily, are recommended when treatment with other agents has failed (**B-II**). Intravenous echinocandin or AmB-d at a dosage of 0.3 mg/kg daily can be used in treating patients with refractory disease (**B-II**).
63. Chronic suppressive therapy is usually unnecessary for patients with human immunodeficiency virus (HIV) infection (**A-I**). If suppressive therapy is required, fluconazole at a dosage of 100 mg 3 times weekly is recommended (**A-I**). Treatment with highly active antiretroviral therapy (HAART) is recommended to reduce recurrent infections (**A-I**).
64. For denture-related candidiasis, disinfection of the denture, in addition to antifungal therapy, is recommended (**B-II**).

Recommendations: Esophageal Candidiasis

65. Systemic antifungal therapy is always required (**A-II**). Oral fluconazole at a dosage of 200–400 mg (3–6 mg/kg) daily for 14–21 days is recommended (**A-I**). Intravenous fluconazole at a dosage of 400 mg (6 mg/kg) daily, AmB-d at a dosage of 0.3–0.7 mg/kg daily, or an echinocandin should be used for

patients who cannot tolerate oral therapy (**B-II**). A diagnostic trial of antifungal therapy is appropriate before performing an endoscopic examination (**B-II**).

66. For fluconazole-refractory disease, itraconazole solution at a dosage of 200 mg daily, posaconazole suspension at a dosage of 400 mg twice daily, or voriconazole at a dosage of 200 mg twice daily administered intravenously or orally for 14–21 days is recommended (**A-III**). Micafungin at a dosage of 150 mg daily, caspofungin at a dosage of 50 mg daily, anidulafungin at a dosage of 200 mg daily, or AmB-d at a dosage of 0.3–0.7 mg/kg daily are acceptable alternatives (**B-II**).
67. Suppressive therapy with fluconazole at a dosage of 100–200 mg 3 times weekly is recommended for recurrent infections (**A-I**).
68. In patients with acquired immunodeficiency syndrome (AIDS), treatment with HAART is recommended to reduce recurrent infections (**A-I**).

Should Antifungal Prophylaxis Be Used for Solid-Organ Transplant Recipients, Intensive Care Unit (ICU) Patients, Neutropenic Patients Receiving Chemotherapy, and Stem Cell Transplant Recipients At Risk of Candidiasis?

69. For solid-organ transplant recipients, fluconazole at a dosage of 200–400 mg (3–6 mg/kg) daily or LAmB at a dosage of 1–2 mg/kg daily, each for at least 7–14 days, is recommended as postoperative prophylaxis for high-risk liver (**A-I**), pancreas (**B-II**), and small bowel (**B-III**) transplant recipients.
70. For ICU patients, fluconazole at a dosage of 400 mg (6 mg/kg) daily is recommended for high-risk patients in adult units with a high incidence of invasive candidiasis (**B-I**).
71. For patients with chemotherapy-induced neutropenia, fluconazole at a dosage of 400 mg (6 mg/kg) daily (**A-I**), posaconazole at a dosage of 200 mg 3 times per day (**A-I**), or caspofungin at a dosage of 50 mg daily (**B-II**) is recommended during induction chemotherapy for the duration of neutropenia. Oral itraconazole at a dosage of 200 mg daily is an effective alternative (**A-I**) but offers little advantage and is less well tolerated than these agents.
72. For stem cell transplant recipients with neutropenia, fluconazole at a dosage of 400 mg (6 mg/kg) daily, posaconazole at a dosage of 200 mg 3 times daily, or micafungin at a dosage of 50 mg daily is recommended during the period of risk of neutropenia (**A-I**).

Definitions:

Infectious Diseases Society of America—US Public Health Service Grading System for Ranking Recommendations in Clinical Guidelines

Category/Grade	Definition
Strength of Recommendation	
A	Good evidence to support a recommendation for or against use.
B	Moderate evidence to support a recommendation for or against use.

Category/Grade	Definition
C	Poor evidence to support a recommendation.
Quality of Evidence	
I	Evidence from ≥1 properly randomized, controlled trial.
II	Evidence from ≥1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from >1 center); from multiple time-series; or from dramatic results from uncontrolled experiments.
III	Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Adapted from Canadian Task Force on the Periodic Health Examination.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management of patients who either have or are at risk of invasive candidiasis or mucosal candidiasis

POTENTIAL HARMS

Treatment-related toxicity and adverse effects

- Nephrotoxicity is the most common serious adverse effect associated with amphotericin B deoxycholate therapy, resulting in acute renal failure in up to 50% of recipients.
- Most azoles, including fluconazole, itraconazole, and posaconazole, should generally be avoided in pregnant women because of the possibility of birth defects associated with their use (category C). There are fewer data concerning the echinocandins, but these should be used with caution during pregnancy (category C).

- Because there are unknown risks for neurologic and cognitive disorders after fluconazole exposure in neonates, neurodevelopmental parameters should be followed in neonates who receive this agent.

Refer to the original guideline for further discussion of treatment-related toxicity and adverse effects of antifungal therapy.

CONTRAINDICATIONS

CONTRAINDICATIONS

Flucytosine and voriconazole are contraindicated during pregnancy because of fetal abnormalities observed in animals.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Pappas PG, Kauffman CA, Andes D, Benjamin DK Jr, Calandra TF, Edwards JE Jr, Filler SG, Fisher JF, Kullberg BJ, Ostrosky-Zeichner L, Reboli AC, Rex JH, Walsh TJ, Sobel JD, Infectious Diseases Society of America. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009 Mar 1;48(5):503-35. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Jan 15 (revised 2009 Mar 1)

GUIDELINE DEVELOPER(S)

Infectious Diseases Society of America - Medical Specialty Society

SOURCE(S) OF FUNDING

Infectious Diseases Society of America (IDSA)

GUIDELINE COMMITTEE

Infectious Diseases Society of America (IDSA) Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All members of the Expert Panel complied with the Infectious Diseases Society of America (IDSA) policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Members of the Expert Panel were provided with the IDSA's conflict of interest disclosure statement and were asked to identify ties to companies developing products that might be affected by promulgation of the guidelines. Information was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. The Expert Panel made decisions on a case-by-case basis as to whether an individual's role should be limited as a result of a conflict. Potential conflicts of interest are listed below.

P.G.P. has received honoraria and research grants and has served as a consultant to Schering-Plough, Astellas Pharma, Merck, Novartis, Basilea, and Pfizer Pharmaceuticals.

D.A. has served as an advisor and received honoraria from Pfizer Pharmaceuticals, Merck, and Astellas Pharma and has received research grants from Astellas Pharma, Pfizer Pharmaceuticals, and the National Institutes of Health.

D.K.B. has received research funding from Astellas Pharma, Biosynexus, Associates of Cape Cod, Pfizer, Rockeby, National Institute of Child Health and Human Development, and Thrasher Research Fund and has received organizational grants from AstraZeneca International, Johnson and Johnson, Medicines Company, MedImmune, and Pfizer.

T.C. has served as a consultant to Pfizer Pharmaceuticals, Merck, and Novartis and has received honoraria from Pfizer Pharmaceuticals, Merck, Novartis, Schering Plough, and Roche Diagnostics.

S.G.F. has received research grants from Pfizer, Amgen, and Merck; has received research funding from the National Institutes of Health and Columbia University; has served as a consultant for Theravance, Forest Pharmaceuticals, and Semorex; and holds stock in NovaDigm Therapeutics.

J.F.F. has received honoraria from Pfizer Pharmaceuticals, Merck, and Wyeth.

C.A.K. receives royalties from UpToDate and Springer Publisher and has received funding from Merck, the Centers for Disease Control and Prevention, Astellas Pharma, and Romark Laboratories.

B.-J.K. has served as a consultant or advisor to Basilea Pharmaceutica, Novartis, Pfizer Pharmaceuticals, and Schering-Plough and has received honoraria from MSD, Pfizer Pharmaceuticals, and Schering-Plough.

L.O.-Z. has served as a consultant for Astellas Pharma, Merck, Pfizer Pharmaceuticals, and Viracor; has received honoraria from Gilead, Merck, Pfizer, and Astellas Pharma; and has received research grants from Merck, Pfizer Pharmaceuticals, Astellas Pharma, Basilea Pharmaceutica, Associates of Cape Cod, and Viracor.

A.C.R. has served as a consultant or advisor for Pfizer Pharmaceuticals, Astellas Pharma, and Merck; has received honoraria from Pfizer Pharmaceuticals; and has received research grants from Pfizer Pharmaceuticals and Merck.

J.E.E. has received research funding from Schering-Plough, Schering, Enzon, Merck, Basilea Pharmaceutica, Pfizer Pharmaceuticals, Astellas Pharma, and Cubist Pharmaceuticals; has been on the scientific advisory boards of Merck, Pfizer, Gilead, Enzon, Cerexa, and Calixia; and is a founder of NovaDigm Therapeutics.

J.D.S. has received honoraria from Pfizer Pharmaceuticals, Merck, and KV Pharmaceuticals; has received research funding from Pfizer Pharmaceuticals,

Merck, and Astellas Pharma; and has served as a consultant for Merck, Pfizer, and Embil.

T.J.W. has received research funding from Astellas Pharma and Vicuron through the Cooperative Research and Development Agreement.

J.F.R. is an employee of Astra Zeneca.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Pappas PG, Rex JH, Sobel JD, Filler SG, Dismukes WE, Walsh TJ, Edwards JE. Guidelines for treatment of candidiasis. Clin Infect Dis 2004 Jan 15;38(2):161-89. [344 references]

GUIDELINE AVAILABILITY

Electronic copies: Available from the Infectious Diseases Society of America (IDSA) Web site.

Print copies: Available from Dr. Peter G. Pappas, Dept. of Medicine, Div. of Infectious Diseases, University of Alabama at Birmingham, 1900 University Blvd, THT 229, Birmingham, Alabama 35294-0006 (pappas@uab.edu).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Kish MA. Guide to development of practice guidelines. Clin Infect Dis 2001 Mar 15;32(6):851-4.

Electronic copies: Available from the Clinical Infectious Diseases Journal Web site.

Print copies: Available from Infectious Diseases Society of America, 1300 Wilson Boulevard, Suite 300, Arlington, VA 22209.

A Personal Digital Assistant (PDA) version of the guideline is available from the Infectious Diseases Society Web site.

Additionally, suggested performance measures are provided in the original guideline document.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on May 1, 2001. The information was verified by the guideline developer on June 29, 2001. This summary was updated by ECRI on April 20, 2004. This summary was updated by ECRI Institute on February 26, 2008 following the U.S. Food and Drug Administration advisory/voluntary market withdrawal of the liquid formulation of Leukine (sargramostim). This summary was updated by ECRI Institute on March 26, 2009. The updated information was verified by the guideline developer on May 5, 2009.

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